CLAIMS

1. Process for modulating the function of a DNA element in a eukaryotic cell,
comprising the step of contacting a genomic DNA element, so-called " chromatin responsive element " (CRE),
with a compound having a molecular weight of less than approximately 5 KDa, and having the capacity to bind in a_sequence-specific manner to said CRE,
said step of contacting being carried out in conditions permitting chromatin remodeling of the CRE by said compound,
wherein said chromatin remodeling of the CRE alters the activity of one or more other DNA elements, so called " modulated DNA elements " in the genome.

2. Process according to claim 1 wherein the chromatin remodeling involves altering the epigenetic state of the CRE and / or other DNA elements.

3. Process according to claim 1 wherein the CRE or the other DNA element(s) comprises heterochromatin, heterochromatin-like DNA, euchromatin or naked DNA.

4. Process according to claim 3 wherein the CRE comprises single copy DNA or multicopy DNA

5. Process according to claim 4 wherein the CRE contains identical or non-identical sequence motifs, or functionally interacting multipartite DNA segments.

6. Process according to claim 3 wherein the CRE comprises a DNA element involved in chromosome structure and function.

7. Process according to claim 5 wherein the CRE comprises satellite DNA.

8. Process according to claim 6 wherein the other DNA element comprises a regulatory DNA element.

9. Process according to claim 1, 2 or 3 wherein the CRE is cis-acting with respect to said other DNA element(s), in either a local or long-range manner.

10. Process according to claim 5 wherein the CRE is cis-acting and is contained within said other DNA element.

11. Process according to any one of claims 1 to 4 wherein the CRE is trans-acting in that the other DNA element(s) is or are not directly linked to the CRE.

12. Process according to claim 1 wherein the modulation gives rise to one or more of the following effects : restoration of chromosome function, loss of chromosome function, enhancement of chromosome function, reduction of chromosome function, prevention of chromosome function, modification of the temporal or spatial specificity of gene function, and maintenance of chromosome function.

13. Process according to claim 12 wherein the modulation gives rise to restoration of gene function by suppression of *cis or trans* epigentic gene silencing.

14. Process according to claim 12 wherein the modulation gives rise to loss of gene function by redistribution, displacement or inhibition of euchromatic binding factors involved in chromosome function, or by allowing the binding of such factors.

15. Process according to any one of claims 1 to 14 wherein the other DNA element(s) is (are) endogenous to said cell.

16. Process according to any one of claims 1 to 14 wherein the other DNA elements(s) is (are) heterologous to said cell.

17. Process according to claim 15 or 16 wherein the CRE is endogenous to said cell.

18. Process according to claim 15 or 16 wherein the CRE is heterologous to said cell.

19. Process according to claim 1 which is carried out *in vivo*, *in vitro* or *ex vivo*.

20. Process according to any one of claims 1 to 19, wherein the sequence-specific DNA binding compound binds to the DNA minor groove.

21. Process according to any one of claims 1 to 20 wherein the sequence-specific DNA binding compound is cell-permeable.

22. Process according to claim 20 or 21 wherein said compound has an apparent binding affinity of at least $5 \times 10^7 M^{-1}$.

23. Process according to claim 22 wherein said compound has an apparent binding affinity of at least $1 \times 10^9 M^{-1}$.

24. Process according to claim 23 wherein said compound has an apparent binding affinity of at least $5 \times 10^{10} M^{-1}$

25. Process according to claim 1 wherein the sequence-specific DNA binding compound has the capacity to specifically recognise a sequence of at least 6 nucleotides.

26. Process according to claim 20 wherein said compound is an oligomer comprising organic heterocycles.

27. Process according to claim 26 wherein said heterocycles. having at least one annular nitrogen, oxygen or sulphur.

28. Process according to claim 27 wherein said oligomer includes heterocycles chosen from pyrrole, imidazole, triazole, pyrazole, furan, thiazole, thiophene, oxazole, pyridine, or derivatives of any of these compounds wherein the ring NH group is substituted.

29. Process according to claim 28 wherein the heterocyclic oligomer contains N-methylpyrrole (Py) and / or N-methylimidazole (Im).

30. Process according to claim 28 or 29 wherein the heterocyclic oligomer further contains aliphatic amino acids such as β-alanine and γ-aminobutyric acid.

31. Process for modulating the epigenetic state of a heterologous gene in a cell, said process comprising the steps of :

- transforming said cell with a nucleic acid sequence comprising said heterologous gene, and with a nucleic acid sequence comprising a so-called heterologous " chromatin responsive element " (CRE),
- introducing into said cell a compound which has the capacity to bind in a sequence-specific manner to said heterologous CRE,

said step of contacting being carried out in conditions permitting chromatin remodeling of the heterologous CRE by said compound,

wherein said chromatin modelling of the CRE modulates the epigenetic state of the heterologous gene.

32. Process according to claim 28, wherein the heterologous CRE comprises a sequence whose chromatin status allows the modulation of chromosome function in cis or trans.

33. Process according to claim 31, wherein said cell is eukaryotic.

34. Process according to claim 31, wherein said cell is prokaryotic.

35. Process according to claim 33, wherein said cell is a vertebrate cell, an invertebrate cell, a plant cell.

36. Process according to claim 35, wherein said cell is a mammalian cell, an insect cell, or a yeast cell.

37. Process according to claim 31 wherein the heterologous CRE comprises a SAR-like sequence.

38. Process according to claim 31 wherein the heterologous CRE comprises a GAGAA repeat sequence.

39. Gene expression kit suitable for modulating the epigenetic state of a heterologous gene in a cell, said kit comprising :

- a nucleic acid molecule comprising said heterologous gene ;
- a nucleic acid molecule comprising a so-called heterologous " CRE ", said heterologous CRE being a sequence whose chromatin status allows the modulation of chromosome function in cis or trans ;
- a compound having a molecular weight of less than approximately 5 KDa, and having the capacity to bind in a sequence-specific manner to said CRE.

40. Kit according to claim 39 wherein the heterologous CRE comprises a SAR-like AT tract.

41. Kit according to claim 39 wherein the heterologous CRE comprises a GAGAA repeat sequence.

42. Kit according to claim 39 for use in gene therapy.

43. Cell containing a compound having a molecular weight of less than 5KDa, and having the capacity to bind in a sequence-specific manner to a genomic CRE, said CRE being a sequence whose chromatin status allows the modulation of chromosome function in cis or trans.

44. Cell according to claim 43, wherein said compound specifically binds the DNA-minor groove.

45. Cell according to claim 43 or 44, additionally containing

- a nucleic acid molecule comprising a heterologous gene ;
- a nucleic acid molecule comprising a so-called heterologous " CRE ", said heterologous CRE being a sequence whose chromatin status allows the modulation of chromosome function in cis or trans.

46. Cell according to claim 43 which is a eukaryotic cell.

47. Non-human organism comprising a cell according to claim 43.

48. Organism according to claim 47 which is a non-human animal.

49. Organism according to claim 48 which is a transgenic, non-human animal.

50. Organism according to claim 47 which is a plant.

51. Organism according to claim 50 which is a transgenic plant.

52. Compound having the capacity to bind, in a sequence-specific manner, to a predetermined CRE, said CRE being a sequence whose chromatin status allows modulation of chromosome function in cis or in trans, with the proviso that said compound is not distamycin, HMG-I/Y, or MATH20.

53. Compound having a molecular weight of less than 5KDa and having the capacity to bind, in a sequence-specific manner, to a predetermined CRE, said CRE being a sequence whose chromatin status allows modulation of chromosome function in cis or in trans, said compound having the capacity to specifically recognise a sequence of at least 6 nucleotides.

54. Compound according to claim 53 having the capacity to specifically recognise a sequence of at least 8 nucleotides.

55. Pharmaceutical composition comprising a compound having the capacity to bind, in a sequence-specific manner, to a predetermined CRE, said CRE being a sequence whose chromatin status allows modulation of chromosome function in cis or in trans, in association with a physiologically acceptable excipient, with the proviso that said compound is not distamycin, HMG-I/Y or MATH20.

56. Pharmaceutical composition comprising a compound having a molecular weight of less than 5kDa, and having the capacity to bind, in a sequence-specific

manner, to a predetermined CRE having at least 6 nucleotides, and said CRE being a DNA sequence whose chromatin status allows modulation of chromosome function in cis or in trans, in association with a physiologically acceptable excipient.

57. Association of pharmaceutical compositions, comprising a first pharmaceutical composition containing

- a nucleic acid molecule comprising a heterologous gene ;
- a nucleic acid molecule comprising a so-called heterologous " CRE ", said heterologous CRE being a sequence whose chromatin status allows the modulation of chromosome function in cis or trans, said nucleic acid molecules being in association with a physiologically acceptable excipient, and

a second pharmaceutical composition comprising a compound having the capacity to bind, in a sequence-specific manner, to said CRE, in association with a physiologically acceptable excipient.

58. Association of pharmaceutical compositions according to claim 57, the CRE binding compound in said second pharmaceutical composition has a molecular weight of less than 5kDa.

59. Composition comprising a compound having the capacity to bind, in a sequence-specific manner, to a predetermined CRE having at least 6 nucleotides, said CRE being a DNA sequence whose chromatin status allows modulation of gene function in cis or in

trans, for use in therapy, with the proviso that said compound is not distamycin, HMG-I/Y, or MATH20.

60. Composition comprising a compound having a molecular weight of less than 5kDa, and having the capacity to bind, in a sequence-specific manner, to a predetermined CRE having at least 6 nucleotides, said CRE being a DNA sequence whose chromatin status allows modulation of gene function in cis or in trans, for use in therapy.

61. Association of compositions according to claim 57 or 58, for use in therapy.

62. Association of compositions according to claim 57 or 58, for use in therapy of genetic disorders resulting from epigenetic status.

63. Use of a compound according to any one of claims 52 to 54 in the preparation of a medicament for the treatment of genetic disorders arising from epigenetic status.

64. Use of an association of compositions according to claim 47 in the preparation of a medicament for the treatment of genetic disorders arising from epigenetic status

65. Use according to claim 63 or 64 wherein the disorder is fragile X syndrome, Prader-Willi syndrome or Wilm's tumour.

66. Use of a kit according to claim 39 for the non-therapeutic modulation of expression of heterologous genes in eukaryotic cells.

67. Use according to claim 66 wherein the modulation is carried out in eukaryotic cells in culture.

68. Use according to claim 66 wherein the modulation is carried out in transgenic animals or in transgenic plants.

69. Compound according to claim 52 to 54 which is fluorescent or fluorescently labelled.

70. DNA-binding compound capable of sequence specific binding to genomic DNA, said compound being an oligomer comprising cyclic heterocycles having at least one annular nitrogen, and optionally at least one aliphatic amino acid residue, wherein said compound is fluorescent or fluorescently labelled.

71. Compound according to claim 69 or 70 wherein the fluorescent label is a fluorescent dye such as fluorescein, dansyl, Texas red, isosulfan blue, ethyl red, malachite green, rhodamine and cyanine dyes.

72. Use of a compound according to claim 69 for probing the epigenetic state and location of DNA in chromosomes and nuclei.

73. Use according to claim 70 for diagnosis of pathological conditions arising from epigenetic status.

74. Use according to claim 73 for pre-symptomatic diagnosis of pathological conditions arising from epigenetic status.

75. Use of a compound according to claim 70 or 71 for chromosome visualisation and marking in diagnosis, forensic studies, affiliation studies, or animal husbandry

76. Method for identifying CREs in a genome, said method comprising :

- contacting genomic DNA containing a DNA element whose function is to be modulated, with a series of compounds having the capacity to bind in a sequence specific manner to DNA elements situated upstream, downstream or within the DNA element to be modulated,
- selection of those compounds capable of modulating the epigenetic state of the DNA element to be modulated, for example using chromatin probes such as nucleases.